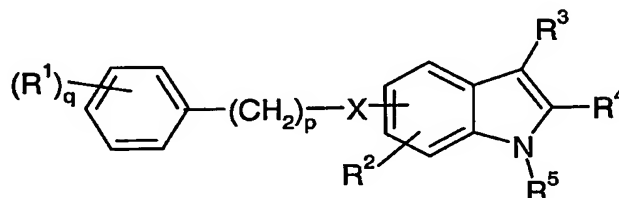


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**Claims**

1. The use of a compound of Formula (I), for the manufacture of a medicament to inhibit and/or reverse and/or alleviate symptoms of angiogenesis and/or any disease state associated with angiogenesis,



Formula (I)

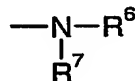
wherein:

R<sup>1</sup> is independently selected from halo, hydroxy, amino, alkanoylamino, —OPO<sub>3</sub>H<sub>2</sub>, or C<sub>1-4</sub>alkoxy, wherein the amino group is optionally substituted by an amino acid residue and the hydroxy group is optionally esterified;

X is selected from: —O—, —S—, —SO— or —SO<sub>2</sub>—;

R<sup>2</sup> is selected from: hydrogen, C<sub>1-4</sub>alkyl or C<sub>1-4</sub>alkoxy;

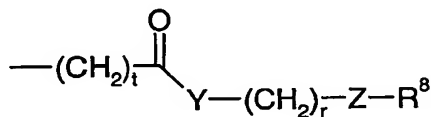
R<sup>3</sup> and R<sup>4</sup> are independently selected from: hydrogen, C<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkanoyl, C<sub>1-4</sub>alkoxycarbonyl, C<sub>1-4</sub>alkoxycarbonylC<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkoxycarbonylamino, amino, aminoC<sub>1-4</sub>alkyl, carbamoyl, carbamoylC<sub>1-4</sub>alkyl, cyano, cyanoC<sub>1-4</sub>alkyl, hydroxy, hydroxyC<sub>1-4</sub>alkyl, or a group of Formula (II):



Formula (II)

R<sup>6</sup> is hydrogen or C<sub>1-4</sub>alkyl;

R<sup>5</sup> and R<sup>7</sup> are independently selected from hydrogen, C<sub>1-4</sub>alkyl or a group of Formula (III):



Formula (III)

wherein Y is selected from —NH—, —O— or a bond;

Z is selected from —NH—, —O—, —C(O)— or a bond;

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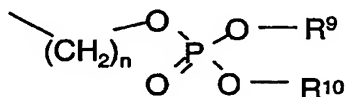
**r** is an integer from 0 to 4;

t is an integer from 0 to 1;

**R<sup>8</sup> is hydrogen, C<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkoxy, aryl, 5 or 6 membered**

heterocyclyl, 5- or 6-membered heteroaryl, wherein aryl, heteroaryl

5 or heterocyclyl are optionally substituted by C<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkoxy, or a group of Formula (IV):



Formula (IV)

wherein n is an integer from 1 to 6, and;

10  $R^9$  and  $R^{10}$  are independently selected from hydrogen,  
C<sub>1-4</sub>alkyl or aryl;

$p$  is an integer from 0 to 1; and

**q** is an integer from 0 to 3;

with the proviso that:

- 15 (i) when R<sup>3</sup> is cyano then R<sup>4</sup> cannot be a group of Formula (II), and  
(ii) when q is 0, R<sup>3</sup> is cyano and X is —S— then R<sup>4</sup> is other than amino;  
or a salt, pro-drug or solvate thereof.

2. The use of a compound of Formula (I), or a salt, pro-drug or solvate thereof, according to Claim 1 wherein:  $R^1$  is hydroxy, amino,  $-OPO_3H_2$ , or  $C_{1-4}$ alkoxy, wherein the amino group is optionally substituted by an amino acid residue and the hydroxy group is optionally esterified.
3. The use of a compound of Formula (I), or a salt, pro-drug or solvate thereof, according to either Claim 1 or Claim 2 wherein: X is  $-O-$  or  $-S-$ .
4. The use of a compound of Formula (I), or a salt, pro-drug or solvate thereof, according to any one of the preceding claims wherein:  $R^3$  is cyano.
5. The use of a compound of Formula (I), or a salt, pro-drug or solvate thereof, according to Claim 1 wherein:
- $R^1$  is selected from hydroxy, amino,  $-OPO_3H_2$ , or  $C_{1-4}$ alkoxy, wherein the amino group is optionally substituted by an amino acid residue;

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$R^2$  is hydrogen;

X is selected from: —O—, —S—, —SO— or —SO<sub>2</sub>—;

p is 0 or 1;

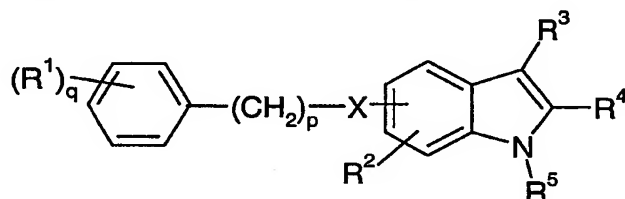
q is an integer from 1 to 3;

5  $R^3$  is selected from: hydrogen, cyano, carbamoyl, carbamoylC<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkanoy, or C<sub>1-4</sub>alkoxycarbonyl;

$R^4$  is selected from: hydrogen, cyano or carbamoyl; and

$R^5$  is hydrogen or C<sub>1-4</sub>alkyl.

6. The use of a compound of Formula (V) as a medicament,



Formula (V)

wherein:

q is from 1 to 3; and

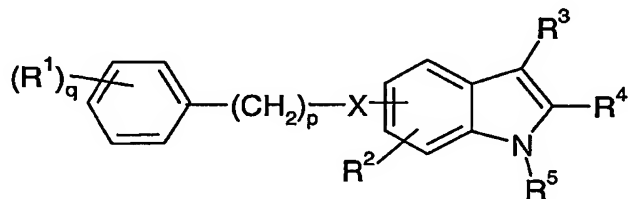
$R^1$ ,  $R^2$ ,  $R^3$ ,  $R^4$ ,  $R^5$ , X and p are as defined in Claim 1,

15 with the proviso that:

- (i) when  $R^3$  is cyano then  $R^4$  cannot be a group of Formula (II); and
- (ii) when  $(R^1)_q$  is 4-methoxy, 4-amino, or 3,4,5-trimethoxy, p is 0 or 1,  $R^2$  is hydrogen or 5-methoxy,  $R^3$  is hydrogen, cyanomethyl or 2-aminoethyl,  $R^4$  is hydrogen or ethoxycarbonyl then  $R^5$  cannot be hydrogen or methyl;

20 or a salt, pro-drug or solvate thereof.

7. A compound of Formula (VIIId),



Formula (VIIId)

wherein:

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$R^1$  is independently selected from hydroxy, amino, alkanoylamino,  $-\text{OPO}_3\text{H}_2$ , or  $\text{C}_{1-4}$ alkoxy, wherein the amino group is optionally substituted by an amino acid residue and the hydroxy group is optionally esterified;

$X$ ,  $p$ ,  $R^2$ ,  $R^3$ ,  $R^4$ , and  $R^5$  are as defined in Claim 1;

5  $q$  is an integer from 1 to 3;

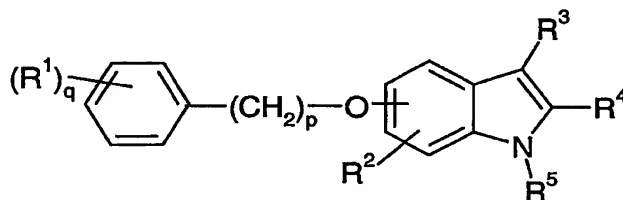
with the proviso that

(i) when  $R^3$  is cyano then  $R^4$  cannot be a group of Formula (II); and

(ii) when  $(R^1)_q$  is 4-methoxy, 4-amino or 3,4,5-trimethoxy,  $p$  is 0 or 1,  $R^2$  is hydrogen or 5-methoxy,  $R^3$  is hydrogen, cyanomethyl or 2-aminoethyl,  $R^4$  is

10 hydrogen or ethoxycarbonyl, then  $R^5$  cannot be hydrogen or methyl; or a salt, pro-drug or solvate thereof.

8. A compound of Formula (VI), according to Claim 7;



Formula (VI)

wherein:

$q$  is from 1 to 3;

$p$ ,  $R^1$ ,  $R^2$ ,  $R^3$ ,  $R^4$ , and  $R^5$  are as defined in Claim 7;

with the proviso that

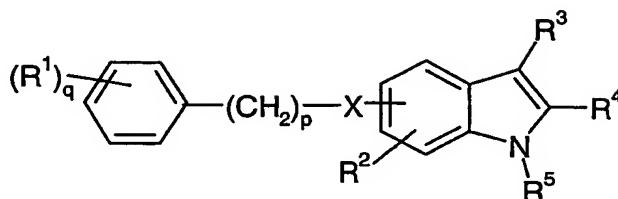
20 (i) when  $R^3$  is cyano then  $R^4$  cannot be a group of Formula (II);

(ii) when  $(R^1)_q$  is 4-methoxy, 4-amino, or 3,4,5-trimethoxy,  $p$  is 0 or 1,  $R^2$  is hydrogen or 5-methoxy,  $R^3$  is hydrogen, cyanomethyl or 2-aminoethyl,  $R^4$  is hydrogen or ethoxycarbonyl then  $R^5$  cannot be hydrogen or methyl;

or a salt, pro-drug or solvate thereof.

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9. A compound of Formula (VIIc), according to Claim 7;



Formula (VIIc)

wherein:

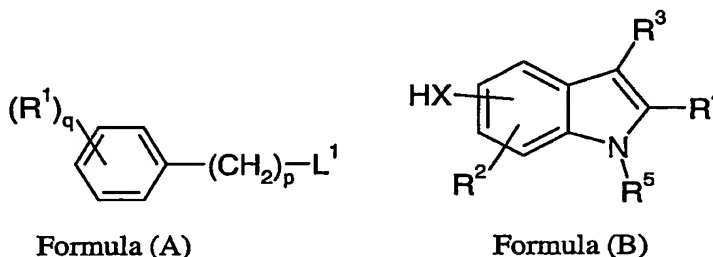
- 5 X is selected from: —S—, —SO— or —SO<sub>2</sub>—;  
 and wherein: p, q, R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup>, and R<sup>5</sup> are as defined in Claim 7;  
 with the proviso that  
 (i) when R<sup>3</sup> is cyano then R<sup>4</sup> cannot be a group of Formula (II);  
 (ii) when (R<sup>1</sup>)<sub>q</sub> is 4-amino, p is 0 or 1, R<sup>2</sup> is hydrogen, R<sup>3</sup> is hydrogen, R<sup>4</sup> is  
 10 hydrogen or ethoxycarbonyl, then R<sup>5</sup> cannot be hydrogen;  
 or a salt, pro-drug or solvate thereof.

10. A compound, according to Claim 7, selected from:  
 3-cyano-5-phenylsulphanyl-1*H*-indole;  
 15 3-cyano-5-phenoxy-1*H*-indole;  
 3-cyano-5-(4-hydroxyphenoxy)-1*H*-indole; and  
 2-cyano-5-benzyloxy-1*H*-indole;  
 1-methyl-3-cyano-5-(4-hydroxy-3,5-dimethoxyphenoxy)-1*H*-indole;  
 1-methyl-3-cyano-5-(4-phosphonoxy-3,5-dimethoxyphenoxy)-1*H*-indole;  
 20 3-cyano-5-(3,4-dimethoxyphenylsulphanyl)-1*H*-indole;  
 1-methyl-3-cyano-5-(3,4-dimethoxyphenylsulphanyl)-1*H*-indole;  
 3-cyano-5-(3,4-dimethoxyphenylsulphonyl)-1*H*-indole; and  
 1-methyl-3-cyano-5-(3,4-dimethoxyphenylsulphonyl)-1*H*-indole;  
 or salt, pro-drug or solvate thereof.
- 25 11. A pharmaceutical composition comprising a compound according to any one of  
 Claims 7 to 10 or a pharmaceutically acceptable salt, solvate or pro-drug thereof.

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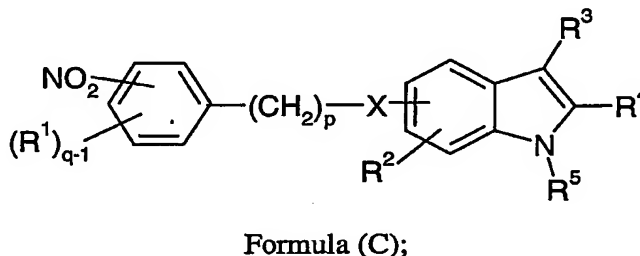
12. A process for preparing a compound of Formula (I), or salt, solvate or pro-drug thereof, which process (wherein  $R^1, R^2, R^3, R^4, R^5, R^6, R^7, R^8, R^9, R^{10}, X, Y, Z, n, p, q, r$  and  $t$  are unless otherwise specified as defined in Claim 1, comprising:

- a) for compounds of Formula (I) wherein  $X$  is  $—O—$ , or  $—S—$ , reacting a  
5 compound of Formula (A) with a compound of Formula (B),

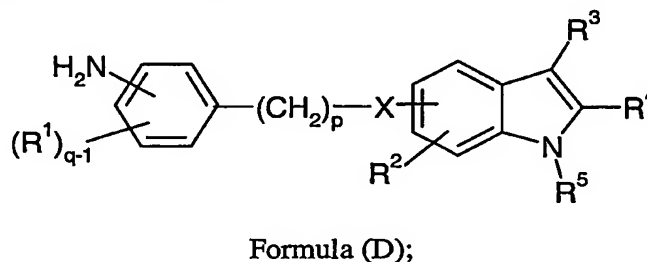


wherein  $L^1$  is a leaving group;

- b) for compounds of Formula (I) in which  $R^1$  comprises amino, reduction of a  
10 compound of Formula (C):

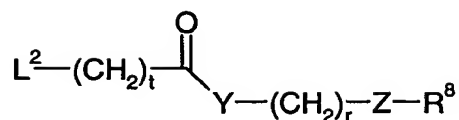


- c) for compounds of Formula (I) wherein  $R^5$  is  $C_{1-4}$ alkyl, reacting a compound of  
Formula (I) wherein  $R^5$  is hydrogen with a suitable alkylhalide;
- 15 d) for compounds of Formula (I) wherein  $R^1$  comprises an amino group substituted by an amino acid residue, reacting a compound of Formula (D) with an amino acid,



- e) for compounds of Formula (I) in which  $R^3$  is a group of Formula (II) and  $R^7$  is a  
20 group of Formula (III), reacting a compounds of Formula (I) in which  $R^3$  is a group of Formula (II) and  $R^7$  is hydrogen with compounds of Formula (E) below, in which  $L^2$  is a leaving group:

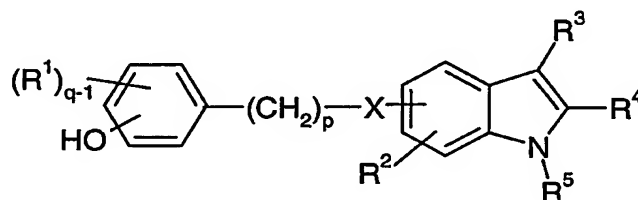
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Formula (E);

f) for compounds of Formula (I) in which  $R^4$  is hydrogen, reacting a compounds of Formula (I) in which  $R^3$  is hydrogen and  $R^4$  is hydrogen with a compounds of  $L^3R^3$  in which  $L^3$  is a leaving group; and

g) for compounds of Formula (I) in which  $R^1$  is an esterified hydroxyl group, reacting a compound of Formula (F) with an appropriate carboxylic acid or carboxylic acid derivative;



Formula (F)

and thereafter if necessary:

- i) converting a compound of Formula (I) into another compound of Formula (I);
- ii) removing any protecting groups;
- iii) forming a salt, pro-drug or solvate.